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(12) UK Patent Application (19) GB (11) 2 206 114 (13) A

(43) Application published 29 Dec 1988

(21) Application No 8814614

(22) Date of filing 20 Jun 1988

(30) Priority data
(31) 8714599 (32) 22 Jun 1987 (33) GB

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(51) INT CL[4]
C07D 405/06 A01N 43/40 // (C07D 405/06 309:32 309:36 213:61)

(52) Domestic classification (Edition J):
C2C 1530 1671 1672 215 247 250 251 253 25Y 28X 313 31Y 337 351 352 355 35X 386 401 40Y 645 675 760 805 80Y AA TZ
U1S 1306 C2C

(56) Documents cited
DE B 1116668

(58) Field of search
C2C

(54) Herbicidal pyridine compounds

(57) Heterocyclic aza–, oxa– or thia–5–cyclohexene–2,4–dione compounds and benzo [b] fused or 5,6–dihydro derivatives thereof, which compounds are substituted in the 3–position by an ortho substituted pyridoyl group and may bear further substituents in the 5– and 6–positions where the heteroring is monocyclic, and in the 1–position where the heteroatom is nitrogen, the process of preparing such compounds, their use in combatting weeds and herbicidal compositions comprising them.

GB 2 206 114 A

Case 130-4011

PYRIDINE COMPOUNDS

The present invention relates to novel aza-, oxa- and thia-5-cyclohexene-2,4-diones and 5,6-dihydro derivatives thereof, the use of such compounds in combatting weeds, novel herbicidal compositions comprising such dione compounds and a process of preparing such novel compounds.

More specifically, the invention relates to novel heterocyclic aza-, oxa- or thia-5-cyclohexene-2,4-dione compounds and benzo [b] fused or 5,6-dihydro derivatives thereof, which compounds are substituted in the 3-position by an ortho substituted pyridoyl group and may bear further substituents in the 5- and 6-positions where the heteroring is monocyclic, and in the 1-position where the heteroatom is nitrogen (hereinafter compounds of formula (A).

The term ortho-substituted pyridoyl as used herein relates to any aryl-CO group wherein aryl is a (2, 3 or 4-) pyridyl, which is substituted in ortho-position of the CO-group. Examples of suitable ortho-substituents are halogen, NO_2, C_{1-4}alkyl, C_{1-4}alkyl-$S(O)_n$ (with n being 0, 1 or 2) or C_{1-4}haloalkyl and C_{2-5}alkenyl. The pyridyl group may bear 1 or 2 further substituents. Examples of such optional additional substituents of the aryl group are halogen, C_{1-4}alkyl, C_{1-4}alkoxy, NO_2, C_{1-4}haloalkyl, cyano, $R_aR_bN(SO_2)_m$ (wherein R_a and R_b independently are H or C_{1-4}alkyl and m is 0 or 1) and hydrocarbyl-$S(O)_{n'}$ (wherein hydrocarbyl is an aliphatic, aromatic or araliphatic group such as C_{1-4}alkyl, phenyl or benzyl which group may be substituted e.g. by halogen or cyano and n' is 0, 1 or 2). Any substituent of the pyridyl moiety in addition to the ortho-substituent is preferably not in ortho'-position of the CO-group. The pyridoyl group is preferably mono-, di-substituted or tri-substituted.

Examples of suitable substituents in the 5-position of the aza-, oxa- or thia-5-cyclohexene-2,4-dione ring or of the 5,6-dihydro derivative of said ring (hereinafter Basic Heteroring) are halogen and C_{1-4}alkyl.

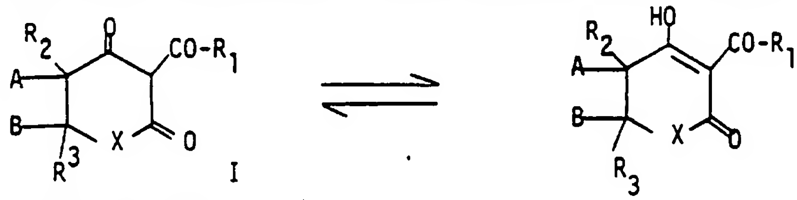
Examples of suitable substituents in the 6-position of the Basic Heteroring are hydrogen, and aliphatic or aromatic hydrocarbyl such as C_{1-4}alkyl, C_{3-6}cycloalkyl or phenyl. The latter phenyl group may be unsubstituted or substituted, e.g. mono or di-substituted; examples of suitable substituents of said phenyl group are C_{1-4}alkyl and halogen.

Where the Basic Heteroring is 5,6-dihydrogenated it may also be disubstituted in the 5- and/or 6-position. Where the 5- and/or 6-position is disubstituted it is e.g. di-C_{1-4}alkylated.

Where the Basic Heteroring comprises N as heteroatom, said ring N-atom may be unsubstituted or substituted. Examples of suitable N-substituents are hydrocarbyl groups such as C_{1-4}alkyl, phenyl or phenyl-alkyl, or unsubstituted or substituted (e.g. by C_{1-4}alkyl) amino.

The compounds of formula (A) are acidic in nature; they may exist in free acid form or in salt form, e.g. alkali or earth alkali metal salt form such as the sodium salt, or in addition salt form, for example with amines such as trialkylamines.

One preferred sub-group of compounds of formula (A) suitable for use in the herbicidal composition of the invention are of formula



I

Ia

wherein X is O, S or NR,

R_1 is pyridyl ortho substituted by halogen, C_{1-4}alkoxy, NO_2, C_{1-4}alkyl, C_{1-4}alkyl-S(O)$_n$ or C_{1-4}haloalkyl or C_{2-5}alkenyl, and optionally bearing one or two additional substituents selected from halogen, C_{1-4}alkyl, C_{1-4}alkoxy, NO_2, C_{1-4}haloalkyl, C_{1-4}haloalkoxy, CN, $R_aR_bN(SO_2)_m$, C_{1-4}alkyl-S(O)$_{n'}$, C_{1-4}alkyl-CO or C_{1-4}alkoxy-CO,

n and n' independently are 0, 1 or 2,

m is 0 or 1

R_a and R_b independently are H or C_{1-4}alkyl,

A and B, independently are H or C_{1-4}alkyl or A and B together form a bond,

R_2 is H, halogen or C_{1-4}alkyl,

R_3 is H, C_{1-4}alkyl, or phenyl which phenyl is unsubstituted or mono- or disubstituted by substituents selected from halogen or C_{1-4}-alkyl, whereby, where A and B together form a bond, R_2 and R_3 may together form a group -CH=CH-CH=CH-,

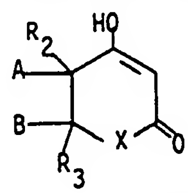
and R is H, C_{1-4}alkyl, phenyl or phenyl-C_{1-4}alkyl.

As shown above, the compounds of formula I may exist in their tautomeric form represented by formula Ia. A similar tautomerism exists of course also for the other compounds of formula (A).

X is preferably O.

The novel compounds of formula (A) and I are obtained by esterification of the corresponding, in 3-position unsubstituted, aza-, oxa- or thia-3,5-cyclohexadiene-2-one-4-ols or -3-cyclohexene-2-one-4-ols with the desired pyridoylhalide, followed by rearrangement of the thus obtained 4-pyridyloxy compound.

This reaction may be illustrated by formulae for the preparation of the compounds of formula I starting from compounds of formula II



II

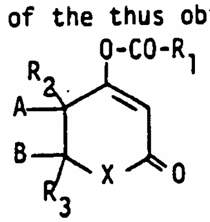
wherein X, R_2, R_3, A and B are as defined above, with a compound of formula III

$$R_1\text{-CO-Hal} \qquad III$$

wherein R_1 is as defined above and

Hal is halogen,

followed by rearrangement of the thus obtained ester of formula IV



IV

wherein X, R_1, R_2,R_3, A and B are as defined above.

The esterification of the 2-one-4-ol compounds with an pyridoylhalide may be effected in a manner known per se for the preparation of esters from an alcohol and an acid halide.

The reaction is conveniently carried out in a solvent which is inert under the reaction conditions, such as dichloromethane, preferably in the presence of an acid binding agent, e.g. such as triethylamine. A suitable reaction temperature lies in the range of from 0° to 40°C, e.g. at 20°C.

The rearrangement of the esters to the desired compounds of formula A can be carried out under the conditions known for the preparation of α-acylated β-diketones from β-ketoenolesters.

Such rearrangement can be carried out in the presence of a Lewis acid catalyst or of a cyanide source such as acetone cyanohydrin with a tertiary amine base.

Suitable Lewis acid catalysts of such rearrangement reaction are for example aluminium chloride or zinc chloride.

Examples of suitable solvents are methylene chloride, acetonitrile or toluene. The reaction temperature is conveniently between 0°C to reflux, preferably at room temperature (about 20°C).

The compounds of formula (A) may be recovered from the reaction mixture in which they are formed by working up by established procedures.

Depending on the reaction conditions the compounds of formula (A) may be obtained in free acid form or in salt form.

The salts of the compounds of formula (A) are obtained from the free acid in a manner known per se, and vice versa.

The starting materials and reagents employed in the process described above are either known or, in the case where they are novel, may be produced by methods analogous to the processes described herein or to known processes.

The hereinabove defined compounds of formula (A), in free acid form or in agriculturally acceptable salt form, in particular the compounds of formula I show interesting broadspectrum herbicidal activity.

The invention relates accordingly also to a method of combatting weeds, comprising applying to the weed locus a herbicidally effective amount of a compound of formula (A) in free acid form or in agriculturally acceptable salt form.

The pre- and post-emergence activity may be shown in greenhouse tests with test dosages equivalent to an application rate of 0.33, 1.0 and 3 kg/ha. The amount of Compound of formula (A) to be applied will depend on the particular weeds to be combatted, the compound employed, its mode of application, conditions of treatment and the like. The appropriate application rate can be determined by routine procedures by those skilled in the

art, or by comparing the activity of the desired compound of formula (A) with standards for which the application rate is known, e.g. in greenhouse tests. In general, satisfactory results are obtained when applying a compound of formula (A) at a rate in the range of from about 0.03 to 3.0 kg/ha plant locus.

The compounds of formula (A) may be and preferably are employed as herbicidal compositions in association with agriculturally acceptable diluent(s). Suitable formulations contain from 0.01% to 99% by weight of active ingredient, from 0 to 20% surfactant and from 1 to 99.99% solid or liquid diluent(s). Higher ratios of surfactant to active ingredient are sometimes desirable and are achieved by incorporation into the formulation or by tank mixing. Application forms of a composition generally contain between 0.01 and 25% by weight of active ingredient. Lower or higher levels of active ingredient can, of course, be present depending on the intended use, the physical properties of the compound and the mode of application. Concentrate forms of a composition intended to be diluted before use generally contain between 2 and 90%, preferably between 10 and 80% by weight of active ingredient.

Useful formulations of the compounds of formula (A) include dusts, granules, suspension concentrates, wettable powders, emulsifiable concentrates, flowables and the like. They are obtained by conventional manner, e.g. by mixing a compound of formula (A) with the diluent(s) and optionally with other ingredients.

Alternatively, the compounds of formula (A) may be used in micro-encapsulated form.

Agriculturally acceptable additives may be employed in the herbicidal compositions to improve the performance of the active ingredient and to reduce foaming, caking and corrosion, for example.

"Surfactant" as used herein means an agriculturally acceptable material which imparts emulsifiability, spreading, wetting, dispersibility or other surface-modifying properties. Examples of surfactants are sodium lignin sulphonate and lauryl sulphate.

"Diluent" as used herein means a liquid or solid agriculturally acceptable material used to dilute a concentrated material to a usable or

desirable strength. For dusts or granules it can be e.g. talc, kaolin or diatomaceous earth, for liquid concentrate forms for example a hydrocarbon such as xylene or an alcohol such as isopropanol, and for liquid application forms i.a. water or diesel oil.

The compositions of this invention can also comprise other compounds having biological activity, e.g. compounds having similar or complementary herbicidal activity or compounds having antidotal, fungicidal or insecticidal activity.

The following examples are provided to illustrate the practice of the invention. Temperature is given in degrees Centigrade. RT means room temperature. Parts and percentages are by weight.

HERBICIDAL COMPOSITIONS

Example A : Wettable Powder

25 Parts of a compound of formula (A), e.g. the compound of Example 1, hereinafter given, are mixed and milled with 25 parts of synthetic fine silica, 2 parts of sodium lauryl sulphate, 3 parts of sodium lignin sulphonate and 45 parts of finely divided kaolin until the mean particle size is about 5 micron.

Example B : Emulsion Concentrate

25 Parts of a compound of formula (A), e.g. the compound of Example 1, hereinafter given, 50 parts of xylene, 15 parts of dimethylformamide and 10 parts of emulsifier are thoroughly mixed until a homogenous solution is obtained.

HERBICIDAL SCREENING

Test Example 1 : Pre-emergence Treatment

Seed pots are filled with a substrate equivalent to a sandy loam. Seeds of Abutilon theophrasti, Amaranthus retroflexus, Sinapis alba, Solanum nigrum, Bromus tectorum, Setaria viridis, Avena fatua and Echinochloa crus-galli are sown in each pot.

The test substance of formula (A) is then applied at a rate corresponding with 1 and 4 kg active ingredient per ha and employing an application volume corresponding with 1000 litre per ha; (sprayed with an aqueous test liquid formulated e.g. in accordance with Example B). After application the seeds are covered with a thin layer (ca. 0.5 cm) of substrate. The pots are kept for 21 days at room temperature (20°-24°) with 14 to 17 hours light (daylight or its equivalent) per day.

Determination of the herbicidal effect is made after the 21 day period. The determination involves visual evaluation of the degree and quality of damage to the various seed plants.

Herbicidal activity is observed.

Test Example 2 : Post-emergence treatment

A procedure similar to that employed in Test Example 1 is followed with the exception that the test compounds are applied when the plants are at the 2-4 leaf stage. The other experimental conditions (application rate, application volume, temperature, light) and evaluation procedure (21 days after application) are as described in Test Example 1.

Herbicidal activity is observed.

Test Example 3

Similar tests as described in Test Examples 1 and 2 are run with various monocotyledonous and dicotyledonous weeds employing various concentrations of test liquid, whereby the concentrations are selected such that the desired application rates are realised. The application volume corresponds with 600 litre/ha.

The evaluation is carried out 28 days after application. Herbicidal activity is observed at application rates of from 30 to 1000 g/ha.

FINAL COMPOUNDS

Example 1: 3-(3,5-Dichloro-2-pyridoyl)-4-hydroxy-6-methyl-2-pyrone

To a suspension of 4.00 g of 3,5-dichloro-2-pyridoylchloride and 2.40g of 4-hydroxy-6-methyl-2-pyrone in 80 ml CH_2Cl_2, was added 1.8 ml triethylamine dropwise, at room temperature. After the exotherm reaction subsided, the mixture was stirred for 6 hrs at room temperature. Then, 2.8 ml triethylamine, followed by 0.7 ml acetone cyanohydrin were added and the resulting solution was stirred overnight.

The reaction mixture was extracted with 1M NaOH. The aqueous extract was washed with CH_2Cl_2, then acidified to pH 3 (1M HCl) and extracted with three portions of CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with water, dried over $MgSO_4$, filtered, and evaporated in vacuo to yield crude solid product. This solid was recrystallized from CH_2Cl_2 and diethyl ether to afford 1.28 g of white crystals with a m.p. 166-168°C, which was consistent with the desired structure by ^1H NMR.

Elemental Analysis: (theory %) C 48.0; H 2.4; N 4.7; Cl 23.6
(found %) C 47.9; H 2.3; N 4.7; Cl 24.2

Example 2

Analogous to the procedure of Example 1, employing the corresponding starting materials of formulae II and III, the following compounds of formula I are obtained (Table I).

Table I: Compounds of formula I wherein
R_1 is 3,5-dichloro-2-pyridoyl and
X is O

Cpd.	A	B	R_2	R_3	Characterisation m.p.
2.1	H	CH_3	H	CH_3	127-128°
2.2	bond (A + B)		H	CH_3	166-168°
2.3	CH_3	CH_3	CH_3	CH_3	

INTERMEDIATES

3,5-Dichloro-2-pyridoylchloride is obtained from 2,3,5-trichloropyridine (Compound V) by the following route.

Example 3: **2-[CH($COOC_2H_5$)$_2$]-3,5-Dichloropyridine (Compound VI)**

To a suspension of 10.4 g 80 % NaH (in mineral oil) in 500 ml N,N-dimethylformamide under nitrogen, was added dropwise, a solution of 45.0 g diethyl malonate in 100 ml N,N-dimethylformamide at room temperature. After the addition was complete, the resulting mixture was stirred for 15 min. at room temperature, then for 30 min. at 50°C. To this mixture was added a solution of 45.7 g 2,3,5-trichloropyridine in 100 ml N,N-dimethylformamide, and stirred overnight at 50°C.

The solvent was evaporated in vacuo, taken up in CH_2Cl_2, washed with four portions of water, dried over $MgSO_4$, filtered, and evaporated in vacuo. The resulting liquid was chromatographed on silica gel with hexane/ethyl acetate 9:1. The product containing fractions were contaminated with diethyl malonate, so these were distilled at reduced pressure to yield 25.2 g of pure product with b.p. 103°C 0.018 mmHg (nD^{20} 1.5068). This liquid was consistent with the desired material by ^1H NMR.

Example 4: **3,5-Dichloro-2-methyl-pyridine (Compound VII)**

A suspension of 70.0 g (Compound VI) was heated at 110°C in 2M H_2SO_4 for 17 hrs. The resulting mixture was cooled and extracted exhaustively with CH_2Cl_2. The CH_2Cl_2 extracts were dried over $MgSO_4$, filtered and evaporated in vacuo to yield 37.0 g of a solid with m.p. 43-44°C, consistent with the desired product by ^1H NMR.

Example 5: **3,5-Dichloropyridine-2-carboxylic acid (Compound VIII)**

To a solution of 1.25 ml aliquat 336 (tricaprylmethylammonium chloride) in 175 ml water, was added 4.00 g 3,5-dichloro-2-methylpyridine, then 19.8% $KMnO_4$ was added. The resulting mixture was heated for 90 min. at 95°C. After cooling to room temperature, the aqueous layer was washed with CH_2Cl_2,

acidified to pH 5 with conc. H_2SO_4, and concentrated to 1/3 volume in vacuo. This solution was then further acidified to pH 1 and a white precipitate was collected by filtration. This material (0.95 g) had m.p. 152°C and was consistent with the desired product by ^1H NMR.

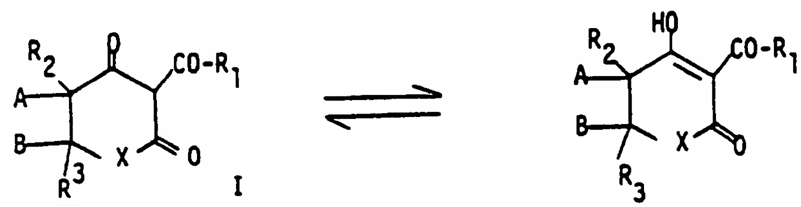
Example 6: 3,5-Dichloro-2-pyridoylchloride

A suspension of 14.3 g 3,5-dichloropyridine-2-carboxylic acid in 60 ml thionyl chloride was heated for 5 hrs at reflux, at which time, solution occurred. The cooled solution was evaporated in vacuo to yield 15.7 g of a white solid with m.p. 58-60°C, consistent with the desired structure by ^1H NMR.

CLAIMS

1. Heterocyclic aza-, oxa- or thia-5-cyclohexene-2,4-dione compounds and benzo [b] fused or 5,6-dihydro derivatives thereof, which compounds are substituted in the 3-position by an ortho substituted pyridoyl group and may bear further substituents in the 5- and 6-positions where the heteroring is monocyclic, and in the 1-position where the heteroatom is nitrogen.

2. Compounds of Claim 1 of formula



I Ia

wherein X is O, S or NR,

R_1 is pyridyl ortho substituted by halogen, C_{1-4}alkoxy, NO_2, C_{1-4}alkyl, C_{1-4}alkyl-$S(O)_n$ or C_{1-4}haloalkyl or C_{2-5}alkenyl, and optionally bearing one or two additional substituents selected from halogen, C_{1-4}alkyl, C_{1-4}alkoxy, NO_2, C_{1-4}haloalkyl, C_{1-4}haloalkoxy, CN, $R_aR_bN(SO_2)_m$, C_{1-4}alkyl-$S(O)_{n'}$, C_{1-4}alkyl-CO or C_{1-4}alkoxy-CO,

n and n' independently are 0, 1 or 2,

m is 0 or 1

R_a and R_b independently are H or C_{1-4}alkyl,

A and B, independently are H or C_{1-4}alkyl or A and B together form a bond,

R_2 is H, halogen or C_{1-4}alkyl,

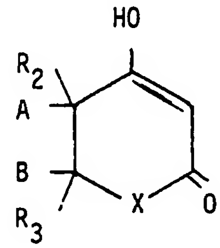
R_3 is H, C_{1-4}alkyl, or phenyl which phenyl is unsubstituted or mono- or disubstituted by substituents selected from halogen or C_{1-4}-alkyl, whereby, where A and B together form a bond, R_2 and R_3 may together form a group -CH=CH-CH=CH-,

and R is H, C_{1-4}alkyl, phenyl or phenyl-C_{1-4}alkyl.

3. Process for the preparation of the dione compounds stated in claim 1, which comprises esterifying aza-, oxa- or thia-5-cyclohexene-2.4-dione compounds which are optionally benzo[b] fused or 5.6-dihydrogenenated and may bear sustituents in the 5- and 6-positions where the cyclodione

is monocyclic, and in the 1-position where the heteroatom is a nitrogen, with an ortho substituted pyridoylhalide, followed by rearrangement of the thus obtained 4-pyridoyloxy compound.

4. The process of claim 3 for the preparation of compounds of formula I, stated in claim 2, which comprises reacting a compound of formula II

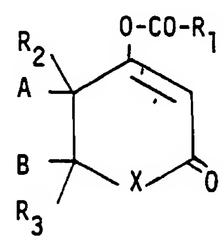


II

wherein X, R_2, R_3, A and B are as stated in claim 2, with a compound of formula III

$$R_1\text{-CO-Hal} \qquad \text{III}$$

wherein R_1 is as stated in claim 2,
followed by rearrangement of the thus obtained 4-pyridoyl ester of formula IV



IV

wherein X, R_1, R_2, R_3, A and B are as stated in claim 2.

5. A herbicide, comprising a compound of Claim 1 or 2.

6. Method of combatting weeds, which comprises applying to the weed locus a herbicidally effective amount of a compound of Claim 1 or 2.

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